```
     (FILE 'HOME' ENTERED AT 10:33:07 ON 28 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 10:33:18 ON 28 JUN 2004
                E NABUMETONE/CN
L1               1 S E2
L2               1 S E3
L3               1 S 76-42-6/RN

     FILE 'CAPLUS' ENTERED AT 10:35:19 ON 28 JUN 2004
L4              23 S L1 AND L3
L5             140 S L1 AND (COX? OR CYCLOOXYGENAS? OR CYCLOXYGENASE? OR SULFONAMI
L6              33 S L5 AND (PAIN? OR ANALGES?)
L7              27 S L6 NOT L4
L8             131 S L1 AND (COX? OR CYCLOOXYGENAS? OR CYCLOXYGENASE?)
L9              31 S L8 AND (PAIN? OR ANALGES?)
L10             25 S L9 NOT L4
L11             36 S L1 AND (OPIAT? OR OPIOID? OR MORPHIN?)
L12             17 S L11 NOT L4
L13            235 S L1 AND (IBUPROFEN?)
L14              8 S L13 AND SYNERG?
L15             54 S L13 AND (ANALGES? OR PAIN?)

     FILE 'EMBASE, BIOSIS, MEDLINE' ENTERED AT 10:59:54 ON 28 JUN 2004
L16           1734 S L1
L17            685 S L16 AND (NSAID?)
L18            226 S L17 AND (PAIN? OR ANALGES?)
L19            739 S (NABUMET? OR RELAFEN? OR RELIFEN? OR RELIFLEX? OR CONSOLAN? O
L20             42 S L18 AND L19
L21             25 DUP REM L20 (17 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 11:05:24 ON 28 JUN 2004

     FILE 'EMBASE, BIOSIS, MEDLINE' ENTERED AT 11:06:51 ON 28 JUN 2004
L22             25 DUP REM L21 (0 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 11:08:53 ON 28 JUN 2004
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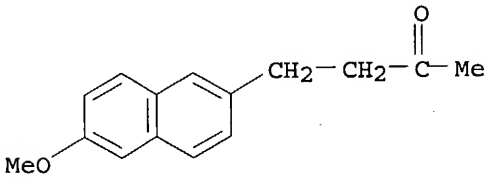
L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 42924-53-8 REGISTRY
CN 2-Butanone, 4-(6-methoxy-2-naphthalenyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-(2'-Methoxynaphth-6'-yl)butan-3-one
CN 4-(6-Methoxy-2-naphthyl)-2-butanone
CN Arthaxan
CN Balmox
CN BRL 14777
CN Consolan
CN Nabumeton
CN **Nabumetone**
CN Nabuser
CN Relafen
CN Relifen
CN Relifex
FS 3D CONCORD
MF C15 H16 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PRP (Properties); USES (Uses)

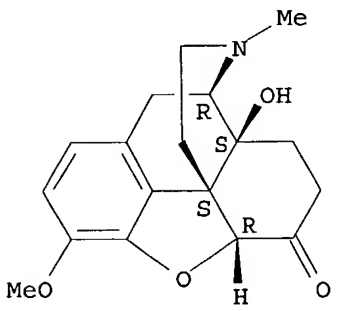


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

539 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
541 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **76-42-6** REGISTRY
CN Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Codeinone, 7,8-dihydro-14-hydroxy- (6CI, 7CI)
CN Morphinan-6-one, 4,5α-epoxy-14-hydroxy-3-methoxy-17-methyl- (8CI)
OTHER NAMES:
CN (-)-Oxycodone
CN 14-Hydroxydihydrocodeinone
CN 3-O-(Methyl)oxymorphone
CN 6-Oxo-14-hydroxy-7,8-dihydrocodeine
CN 7,8-Dihydro-14-hydroxycodeinone
CN Dihydro-14-hydroxycodeinone
CN Dihydrohydroxycodeinone
CN Dihydrone
CN NSC 19043
CN Oxanest
CN Oxicon
CN Oxycodeinone
CN Oxycodone
CN Oxymorphone 3-methyl ether
FS STEREOSEARCH
MF C18 H21 N O4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

728 REFERENCES IN FILE CA (1907 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
732 REFERENCES IN FILE CAPLUS (1907 TO DATE)
32 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:220639 CAPLUS
DN 126:216667
TI Pain-alleviating drug composition and method for alleviating pain
IN Mayer, David J.; Price, Donald D.; Mao, Jianren; Lyle, John W.
PA Virginia Commonwealth University, USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9704780	A2	19970213	WO 1996-US12597	19960731
	WO 9704780	A3	19970327		
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	US 5840731	A	19981124	US 1995-510546	19950802
	CA 2228249	AA	19970213	CA 1996-2228249	19960731
	CA 2228249	C	20021203		
	AU 9666865	A1	19970226	AU 1996-66865	19960731
	EP 845989	A2	19980610	EP 1996-926846	19960731
	EP 845989	B1	20020313		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11512081	T2	19991019	JP 1997-507896	19960731
	AT 214277	E	20020315	AT 1996-926846	19960731
	PT 845989	T	20020731	PT 1996-926846	19960731
	ES 2170865	T3	20020816	ES 1996-926846	19960731
	US 5863922	A	19990126	US 1997-889041	19970707
	US 5869498	A	19990209	US 1997-888728	19970707
PRAI	US 1995-510546	A	19950802		
	WO 1996-US12597	W	19960731		

=> d 23 ab

L4 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AB The analgesic effectiveness of a combination drug containing at least one analgesic is significantly enhanced by the addition of a nontoxic N-methyl-D-aspartate (NMD) receptor antagonist, e.g. dextromethorphan or dextrorphan.

=> d 23 hit

L4 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
IT 50-33-9, Phenylbutazone, biological studies 50-36-2, Cocaine 50-78-2, Aspirin 53-86-1, Indomethacin 57-27-2, Morphine, biological studies 57-42-1, Meperidine 61-68-7, Mefenamic acid 62-67-9, Nalorphine 67-52-7D, Barbituric acid, derivs. 76-41-5, Oxymorphone **76-42-6**, Oxycodone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 103-90-2, Acetaminophen 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 125-71-3, Dextromethorphan 125-73-5, Dextrorphan 152-02-3, Levallorphan 359-83-1, Pentazocine 437-38-7, Fentanyl 465-65-6, Naloxone 466-99-9, Hydromorphone 469-62-5, Propoxyphene 561-27-3, Heroin 644-62-2, Meclofenamic acid 5104-49-4, Flurbiprofen 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16590-41-3, Naltrexone 20594-83-6, Nalbuphine 21256-18-8, Oxaprozin 22071-15-4, Ketoprofen

22204-53-1, Naproxen 22494-27-5, Flufenisal 22494-42-4, Diflunisal
26171-23-3, Tolmetin 29679-58-1, Fenoprofen 33369-31-2, Zomepirac
36322-90-4, Piroxicam 36330-85-5, Fenbufen 38194-50-2, Sulindac
41340-25-4, Etodolac 42408-82-2, Butorphanol **42924-53-8**,
Nabumetone 52485-79-7, Buprenorphine 55096-26-9, Nalmefene
74103-06-3, Ketorolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic compns. containing NMDA antagonists)

L4 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
1998:324821 Document No. 129:23448 Method of modifying angiotensin receptor activity for mediation of pain. Depadova, Anthony S. (USA). U.S. US 5753651 A 19980519, 15 pp., Cont.-in-part of U.S. 5,464,854. (English). CODEN: USXXAM. APPLICATION: US 1996-727553 19961025. PRIORITY: US 1994-235468 19940429; WO 1995-US5312 19950428.

=> d 22 ab

L4 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AB A method for the treatment of acute or chronic pain mediated by the sympathetic nervous system comprises the administration of an effective amount of an AT1 antagonist. The AT1 antagonist can be used alone or in combination with other drug therapies, for instance, non-steroidal anti-inflammatory drugs, antidepressants, opioid drugs, angiotensin converting enzyme inhibitors, and diuretics.

=>

L4 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:742265 CAPLUS
DN 130:10645
TI Cox-2 inhibitors in combination with NMDA blockers for treating pain
IN Caruso, Frank S.
PA Algos Pharmaceutical Corp., USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850075	A1	19981112	WO 1998-US9252	19980506
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9874727	A1	19981127	AU 1998-74727	19980506
PRAI	US 1997-45914P	P	19970507		
	WO 1998-US9252	W	19980506		

AB The analgesic effectiveness of a cyclooxygenase-2 inhibitor is significantly enhanced by administering a cyclooxygenase-2 inhibitor with a nontoxic NMDA receptor antagonist and/or a nontoxic substance that blocks at least one major intracellular consequence of NMDA receptor activation.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN

1998:744954 Document No. 130:17239 Pharmaceutical composition and method combining an antidepressant with an NMDA receptor antagonist, for treating neuropathic pain. Caruso, Frank S. (Algos Pharmaceutical Corp., USA). PCT Int. Appl. WO 9850044 A1 19981112, 22 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US9253 19980506. PRIORITY: US 1997-45900 19970507.

L4 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
1999:126827 Document No. 130:191898 Substance P inhibitors in combination with NMDA blockers for treating pain. Caruso, Frank S. (Algos Pharmaceutical Corporation, USA). PCT Int. Appl. WO 9907413 A1 19990218, 54 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US10707 19980526. PRIORITY: US 1997-55233 19970811.

L12 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1997:332024 Document No. 126:308827 Peripherally active anti-hyperalgesic **opiates**. Yaksh, Tony L.; Farrar, John J.; Maycock, Alan L.; Lewis, Michael E.; Dow, Gordon J. (Regents of the University of California, USA; Adolor Corporation). PCT Int. Appl. WO 9709973 A2 19970320, 317 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US14727 19960912. PRIORITY: US 1995-528510 19950912.

L14 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:126827 CAPLUS
DN 130:191898
TI Substance P inhibitors in combination with NMDA blockers for treating pain
IN Caruso, Frank S.
PA Algos Pharmaceutical Corporation, USA
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9907413	A1	19990218	WO 1998-US10707	19980526
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9876960	A1	19990301	AU 1998-76960	19980526
PRAI	US 1997-55233P	P	19970811		
	WO 1998-US10707	W	19980526		

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:742265 CAPLUS
DN 130:10645
TI Cox-2 inhibitors in combination with NMDA blockers for treating pain
IN Caruso, Frank S.
PA Algos Pharmaceutical Corp., USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850075	A1	19981112	WO 1998-US9252	19980506
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9874727	A1	19981127	AU 1998-74727	19980506
PRAI	US 1997-45914P	P	19970507		
	WO 1998-US9252	W	19980506		

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 47 OF 54 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:377146 CAPLUS
DN 125:49334
TI Composition alleviating **pain**, containing a non-narcotic **analgesic** and an N-methyl-D-aspartate receptor blocker
IN Mayer, David J.; Price, Donald D.; Mao, Jianren; Lyle, John W.
PA Virginia Commonwealth University, USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9607412	A1	19960314	WO 1995-US10994	19950829
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2197463	AA	19960314	CA 1995-2197463	19950829
	AU 9534604	A1	19960327	AU 1995-34604	19950829
	AU 714653	B2	20000106		
	EP 778770	A1	19970618	EP 1995-931016	19950829
	EP 778770	B1	20031210		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1158085	A	19970827	CN 1995-194879	19950829
	HU 76798	A2	19971128	HU 1997-1253	19950829
	BR 9508671	A	19980106	BR 1995-8671	19950829
	JP 10505087	T2	19980519	JP 1995-509560	19950829
	NZ 292429	A	20000128	NZ 1995-292429	19950829
	RU 2213561	C2	20031010	RU 1997-105186	19950829
	AT 255895	E	20031215	AT 1995-931016	19950829
	TW 449474	B	20010811	TW 1995-84109106	19950831
	US 5834479	A	19981110	US 1996-746202	19961106
	FI 9700865	A	19970314	FI 1997-865	19970228
	NO 9700946	A	19970428	NO 1997-946	19970228
PRAI	US 1994-300736	A	19940902		
	US 1995-382063	A	19950201		
	US 1993-27177	A2	19930305		
	US 1993-95107	A2	19930721		
	WO 1995-US10994	W	19950829		

L21 ANSWER 20 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 8

AN 93262026 EMBASE
DN 1993262026
TI Safety experience with **nabumetone** versus diclofenac, naproxen, ibuprofen, and piroxicam in osteoarthritis and rheumatoid arthritis.
AU Eversmeyer W.; Poland M.; DeLapp R.E.; Jensen C.P.
CS Browne McHardy Clinic, 4315 Houma Boulevard,Metarie, LA 70006, United States
SO American Journal of Medicine, (1993) 95/2 A (2A10S-2A18S).
ISSN: 0002-9343 CODEN: AJMEAZ
CY United States
DT Journal; Conference Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LA English
SL English
AB The comparative safety of nabumetone (1,000-2,000 mg/day) versus diclofenac (100-200 mg/day), naproxen (500-1,500 mg/day), piroxicam (10-20 mg/day), and ibuprofen (1,200-3,200 mg/day) was evaluated in a 12-week, randomized, open-label, multicenter study. Patients with osteoarthritis (OA) or rheumatoid arthritis (RA) were enrolled in a 3:1 ratio (nabumetone:one of the four comparator **NSAIDs**). The incidence of ≥1 adverse event considered by the investigator to be related or probably related to therapy was similar in all groups. However, significantly ($p < 0.02$) more diclofenac-treated patients experienced abdominal **pain** and/or gastritis than nabumetone-treated patients. Naproxen-treated patients experienced significantly ($p < 0.002$) more dyspepsia as compared with patients treated with nabumetone or ibuprofen and significantly ($p \leq 0.001$) more nabumetone-treated patients experienced diarrhea than patients treated with naproxen, ibuprofen, or piroxicam. Ulcers occurred in one (0.03%) nabumetone-treated patient versus six (0.5%) patients treated with one of the comparator **NSAIDs** ($p = 0.001$). A decrease in hemoglobin ≥1.5 g/dL occurred in fewer nabumetone-treated patients than in patients treated with diclofenac ($p < 0.04$), ibuprofen ($p \leq 0.04$), or piroxicam ($p = 0.055$). Finally, a similar percentage of patients in all treatment groups withdrew from the study because of adverse events related or probably related to treatment. More ($p < 0.001$) diclofenac-treated patients withdrew because of elevated hepatic transaminases than patients treated with the other agents. Withdrawal because of gastritis was also noted for more diclofenac-treated patients than nabumetone-treated patients ($p < 0.04$). In conclusion, nabumetone was demonstrated to be at least as safe as diclofenac, piroxicam, ibuprofen, and naproxen as related to subjective complaints, such as dyspepsia or gastritis. However, more serious events, such as ulcers or meaningful decreases in hemoglobin, seem to occur less often with nabumetone.

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L21 ANSWER 14 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:164640 BIOSIS
DN PREV199698736775
TI Clinical update of the relative safety of **nabumetone** in long-term clinical trials.
AU Lipani, J. A.; Poland, M.
CS Smithkline Beecham Pharmaceuticals, King of Prussia, PA, USA
SO Inflammopharmacology, (1995) Vol. 3, No. 4, pp. 351-361. ISSN: 0925-4692.
DT Article
LA English
ED Entered STN: 11 Apr 1996
Last Updated on STN: 10 Jun 1997
AB Objective: To determine whether the pharmacological profile of nabumetone results in gastric safety, maintains haemostasis and is renally safe. Methods: The data from seven double-blind trials and one large randomized clinical trial were pooled and subjected to Kaplan-Meier life tests to determine the frequency of perforations, ulcers and bleeds (PUBs). Two studies each examined haemostasis and renal effects in volunteers and patients. Results: PUBs: The cumulative frequency of PUBs with nabumetone was 0.03% in 4471 patients. The cumulative frequency with all other **NSAIDs** comparators ranged from 0.8 to 1.8%. Haemostasis: The mean impedance increased with nabumetone and decreased following indomethacin in normal volunteers. In patients, nabumetone was equivalent to placebo in effect on bleeding time, PT and PPT. Renal effects: In a triple cross-over study in an at-risk population of elderly hypertensive patients receiving ACE/diuretic, nabumetone had no effect on GFR or PGE. Conclusion: The pharmacological profile of nabumetone results in gastric, renal and haemostasis safety.

L21 ANSWER 15 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 94122329 EMBASE
DN 1994122329
TI **Nabumetone**: A clinical appraisal.
AU Helfgott S.M.
CS Brigham and Women's Hospital, 45 Francis St.,Boston, MA 02115, United States
SO Seminars in Arthritis and Rheumatism, (1994) 23/5 (341-346). ISSN: 0049-0172 CODEN: SAHRBF
CY United States
DT Journal; General Review
FS 006 Internal Medicine
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Nonsteroidal antiinflammatory drugs (**NSAIDs**) have long been used as therapy for arthritis patients. However, in some patients these drugs can cause gastrointestinal hemorrhage, perforation, or ulcer through direct topical effects, enterohepatic recirculation, and systemic effects. In an effort to address this problem, new **NSAIDs** have been developed. Nabumetone, which belongs to a new class of **NSAID**, is a nonacidic agent that has been associated with a low incidence of peptic ulcer. This article examines available clinical data on nabumetone, including studies on gastrointestinal safety and effectiveness in osteoarthritis and rheumatoid arthritis patients, and data that may provide an explanation for nabumetone's low incidence of ulceration.

L21 ANSWER 16 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 6

AN 93123898 EMBASE
DN 1993123898
TI **Nabumetone**: A 'nonacidic' nonsteroidal antiinflammatory drug.
AU Dahl S.L.
CS Gold IV Unit M4213, School of Medicine, University of Missouri, 2411 Holmes,Kansas City, MO 64108, United States
SO Annals of Pharmacotherapy, (1993) 27/4 (456-463).
ISSN: 1060-0280 CODEN: APHRER
CY United States
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English; Spanish; French
AB OBJECTIVE: To review the pharmacology, pharmacokinetic disposition, dosage recommendations, adverse effects, drug interactions, and efficacy of nabumetone in patients with selected rheumatic disorders and soft-tissue injuries. DATA SOURCES: Data from scientific literature were extracted, evaluated, and summarized for presentation. A MEDLINE search was conducted using the following indexing terms: antiinflammatory agents, nonsteroidal, nabumetone, rheumatoid arthritis (RA), and osteoarthritis (OA). Studies evaluating nabumetone reported in articles, abstracts, or proceedings involving human subjects were considered for inclusion. STUDY SELECTION: Special consideration was given to clinical studies using double-blind, randomized, parallel, controlled designs. Studies comparing the effectiveness and safety of nabumetone with placebo and other nonsteroidal antiinflammatory drugs (**NSAIDs**) were included. DATA EXTRACTION: Data from human studies published in the English language were evaluated. Trials were assessed according to study design, sample size, and description of outcomes. DATA SYNTHESIS: Nabumetone is a nonacidic prodrug that is metabolized to an active nonsteroidal antiinflammatory moiety, 6-methoxy-2-naphthylacetic acid (6- MNA). 6-MNA is a structural analog of naproxen. Like naproxen and other **NSAIDs**, 6-MNA possesses **analgesic**, antipyretic, and antiinflammatory activity. 6-MNA has a prolonged elimination half-life, ranging from 17 to 74 hours, which allows for once-daily dosing. The efficacy of nabumetone for treating symptoms of RA and OA has been established in controlled clinical trials. Nabumetone also has been studied in ankylosing spondylitis and soft- tissue injuries. Adverse effects associated with nabumetone are similar to those associated with other **NSAIDs**. Gastrointestinal reactions occur most frequently in the form of abdominal **pain** or indigestion, nausea, or vomiting. Central nervous system adverse effects occur less frequently, and are followed in order of occurrence by rashes. CONCLUSIONS: Nabumetone is a prodrug metabolized to an active metabolite structurally related to naproxen. Studies have demonstrated the efficacy of nabumetone, but no advantages over the many other **NSAIDs** now available.

L21 ANSWER 17 OF 25 EMBASE
on STN DUPLICATE 7
AN 93093898 EMBASE
DN 1993093898
TI **Nabumetone**. A reappraisal of its pharmacology and therapeutic use in rheumatic diseases.
AU Friedel H.A.; Langtry H.D.; Buckley M.M.
CS Adis International Limited, 41 Centorian Drive, Priv Bag 65901,Mairangi Bay, Auckland 10, New Zealand
SO Drugs, (1993) 45/1 (131-156).
ISSN: 0012-6667 CODEN: DRUGAY
CY New Zealand
DT Journal; General Review
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index

038 Adverse Reactions Titles
LA English
SL English
AB Nabumetone is a nonsteroidal anti-infammatory drug (**NSAID**) used to treat rheumatic and inflammatory conditions. It is absorbed as a nonacidic prodrug and is rapidly converted in the liver to an active metabolite which is responsible for its anti-inflammatory and **analgesic** effects. Published data from earlier comparative studies indicate that nabumetone, administered in a single dose of 1 to 2g daily, is as effective as aspirin, diclofenac, ibuprofen, indomethacin, naproxen and sulindac for the symptomatic treatment of rheumatoid arthritis, osteoarthritis, various nonarticular rheumatic conditions and acute soft tissue injury. Adverse events with nabumetone occur less frequently than with aspirin, and the incidence of gastrointestinal adverse events with nabumetone compares favourably with that of other **NSAIDs**. Rates of gastrointestinal ulceration and bleeding with nabumetone are low, apparently less than 1% annually. More recently, data from large-scale clinical trials and postmarketing surveillance studies have further confirmed the efficacy and tolerability of nabumetone. Thus, the drug should now be considered a well established member of this group of agents for the treatment of **painful** rheumatic and inflammatory conditions.

L21 ANSWER 18 OF 25 MEDLINE on STN
AN 93362688 MEDLINE
DN PubMed ID: 8356998
TI Efficacy and safety of **nabumetone** versus diclofenac, naproxen, ibuprofen, and piroxicam in the elderly.
AU Morgan G J; Poland M; DeLapp R E
CS Department of Medicine, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire 03756.
SO American journal of medicine, (1993 Aug 9) 95 (2A) 19S-27S.
Journal code: 0267200. ISSN: 0002-9343.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199309
ED Entered STN: 19931008
Last Updated on STN: 19931008
Entered Medline: 19930923
AB In a randomized, open-label, controlled, multicenter, 12-week study, the efficacy and safety of nabumetone (1,000-2,000 mg/day) versus diclofenac (100-200 mg/day), naproxen (500-1,500 mg/day), ibuprofen (1,200-3,200 mg/day), or piroxicam (10-20 mg/day) were evaluated in patients with osteoarthritis (OA) or rheumatoid arthritis (RA). The results in elderly patients (> or = 65 years of age) are presented. Nabumetone was as effective as the comparator nonsteroidal antiinflammatory drugs (**NSAIDs**) in the treatment of elderly OA and RA patients. Ibuprofen and diclofenac caused significantly ($p < 0.05$) more abdominal **pain** than nabumetone (8.5%, 13.1%, and 4.1%, respectively). The frequency of abdominal **pain** was dose related for all **NSAIDs** except nabumetone. Diarrhea was reported by significantly ($p < 0.02$) more nabumetone-treated (6.6%) than ibuprofen-treated (0.9%) elderly patients, but the incidence of diarrhea was not dose related. There were no clinically significant changes in renal function with nabumetone or the comparator **NSAIDs**. A significant change in hepatic enzymes occurred in elderly patients treated with diclofenac (3.3%), which was different than for patients treated with nabumetone ($p < 0.04$), naproxen ($p < 0.06$), or ibuprofen ($p < 0.06$). With regard to withdrawals for adverse events, more ($p < 0.04$) piroxicam-treated patients (4.9%) withdrew

than nabumetone-treated patients (1%). In addition, doubling the dose of nabumetone from 1,000 mg/day to 2,000 mg/day did not result in a proportional increase in adverse events. However, with the comparator **NSAIDs**, proportional increases in adverse events occurred with increased dose. Finally, the efficacy and safety of nabumetone in elderly patients were similar to the efficacy and safety observed in nonelderly patients.

L21 ANSWER 19 OF 25 MEDLINE on STN
AN 93362687 MEDLINE
DN PubMed ID: 8356997
TI Safety experience with **nabumetone** versus diclofenac, naproxen, ibuprofen, and piroxicam in osteoarthritis and rheumatoid arthritis.
AU Eversmeyer W; Poland M; DeLapp R E; Jensen C P
CS Department of Medicine, Browne McHardy Clinic, Metarie, Louisiana 70006.
SO American journal of medicine, (1993 Aug 9) 95 (2A) 10S-18S.
Journal code: 0267200. ISSN: 0002-9343.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199309
ED Entered STN: 19931008
Last Updated on STN: 19931008
Entered Medline: 19930923
AB The comparative safety of nabumetone (1,000-2,000 mg/day) versus diclofenac (100-200 mg/day), naproxen (500-1,500 mg/day), piroxicam (10-20 mg/day), and ibuprofen (1,200-3,200 mg/day) was evaluated in a 12-week, randomized, open-label, multicenter study. Patients with osteoarthritis (OA) or rheumatoid arthritis (RA) were enrolled in a 3:1 ratio (nabumetone:one of the four comparator **NSAIDs**). The incidence of > or = 1 adverse event considered by the investigator to be related or probably related to therapy was similar in all groups. However, significantly ($p < 0.02$) more diclofenac-treated patients experienced abdominal **pain** and/or gastritis than nabumetone-treated patients. Naproxen-treated patients experienced significantly ($p < 0.002$) more dyspepsia as compared with patients treated with nabumetone or ibuprofen and significantly ($p <$ or $= 0.001$) more nabumetone-treated patients experienced diarrhea than patients treated with naproxen, ibuprofen, or piroxicam. Ulcers occurred in one (0.03%) nabumetone-treated patient versus six (0.5%) patients treated with one of the comparator **NSAIDs** ($p = 0.001$). A decrease in hemoglobin > or = 1.5 g/dL occurred in fewer nabumetone-treated patients than in patients treated with diclofenac ($p < 0.04$), ibuprofen ($p <$ or $= 0.04$), or piroxicam ($p = 0.055$). Finally, a similar percentage of patients in all treatment groups withdrew from the study because of adverse events related or probably related to treatment. More ($p < 0.001$) diclofenac-treated patients withdrew because of elevated hepatic transaminases than patients treated with the other agents. Withdrawal because of gastritis was also noted for more diclofenac-treated patients than nabumetone-treated patients ($p < 0.04$). In conclusion, nabumetone was demonstrated to be at least as safe as diclofenac, piroxicam, ibuprofen, and naproxen as related to subjective complaints, such as dyspepsia or gastritis. However, more serious events, such as ulcers or meaningful decreases in hemoglobin, seem to occur less often with nabumetone.

L21 ANSWER 20 OF 25 EMBASE
on STN DUPLICATE 8
AN 93262026 EMBASE
DN 1993262026
TI Safety experience with **nabumetone** versus diclofenac, naproxen,

ibuprofen, and piroxicam in osteoarthritis and rheumatoid arthritis.

AU Eversmeyer W.; Poland M.; DeLapp R.E.; Jensen C.P.
CS Browne McHardy Clinic, 4315 Houma Boulevard,Metarie, LA 70006, United States

SO American Journal of Medicine, (1993) 95/2 A (2A10S-2A18S).
ISSN: 0002-9343 CODEN: AJMEAZ
CY United States
DT Journal; Conference Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LA English
SL English

AB The comparative safety of nabumetone (1,000-2,000 mg/day) versus diclofenac (100-200 mg/day), naproxen (500-1,500 mg/day), piroxicam (10-20 mg/day), and ibuprofen (1,200-3,200 mg/day) was evaluated in a 12-week, randomized, open-label, multicenter study. Patients with osteoarthritis (OA) or rheumatoid arthritis (RA) were enrolled in a 3:1 ratio (nabumetone:one of the four comparator **NSAIDs**). The incidence of ≥1 adverse event considered by the investigator to be related or probably related to therapy was similar in all groups. However, significantly ($p < 0.02$) more diclofenac-treated patients experienced abdominal **pain** and/or gastritis than nabumetone-treated patients. Naproxen-treated patients experienced significantly ($p < 0.002$) more dyspepsia as compared with patients treated with nabumetone or ibuprofen and significantly ($p \leq 0.001$) more nabumetone-treated patients experienced diarrhea than patients treated with naproxen, ibuprofen, or piroxicam. Ulcers occurred in one (0.03%) nabumetone-treated patient versus six (0.5%) patients treated with one of the comparator **NSAIDs** ($p = 0.001$). A decrease in hemoglobin ≥1.5 g/dL occurred in fewer nabumetone-treated patients than in patients treated with diclofenac ($p < 0.04$), ibuprofen ($p \leq 0.04$), or piroxicam ($p = 0.055$). Finally, a similar percentage of patients in all treatment groups withdrew from the study because of adverse events related or probably related to treatment. More ($p < 0.001$) diclofenac-treated patients withdrew because of elevated hepatic transaminases than patients treated with the other agents. Withdrawal because of gastritis was also noted for more diclofenac-treated patients than nabumetone-treated patients ($p < 0.04$). In conclusion, nabumetone was demonstrated to be at least as safe as diclofenac, piroxicam, ibuprofen, and naproxen as related to subjective complaints, such as dyspepsia or gastritis. However, more serious events, such as ulcers or meaningful decreases in hemoglobin, seem to occur less often with nabumetone.